1. Scientific Abstract

The hypothesis of the clinical trial is that the combination of two previously studied vaccines, ALVAC-CEA and vaccinia-CEA, will result in a more potent stimulus to the immune system to recognize and destroy CEA-bearing tumors in patients with advanced CEA-bearing cancers. The two lead investigators, Drs. Marshall and Hamilton, performed the initial phase 1 trials with the two agents under study in this trial. The laboratory and immunologic studies were performed by Dr. Schlom's group in both prior studies and in this one as well.

The objectives of this trial are to evaluate the safety of sequentially administered vaccinia-CEA and ALVAC-CEA in 2 schedules and with addition of GM-CSF plus/minus IL-2, to compare the CEA-specific immune response in cancer patients among the various schedules and treatment regimens, to determine if the addition of GM-CSF or IL-2 enhances the immune response, and finally to compare ELISPOT with more standard monitoring assays for monitoring the lymphoproliferative response.

CEA-bearing tumors such as cancers of the GI tract, breast, and lung are among the most common and most lethal tumors. Systemic therapies developed to date have made only a minor impact on the overall survival and quality of life in patients with these diseases. Therefore, the need for additional, novel therapies is essential. Enhancement of the immune system has long been an attractive target for systemic therapies, but has been a disappointment to date. Few immune-based therapies have clearly shown improved outcomes. Vaccine technology may allow for a more specific enhancement of the immune system with less toxicity, thereby making it useful in a wider scope of patients, such as those with earlier stage disease. Phase 1 clinical trials must precede these larger studies in order to determine the optimum treatment combinations and schedules.

In the first two clinical trials mentioned above, both vaccines alone have shown the ability to alter a patient's ability to recognize and respond to CEA epitopes that did not exist prior to vaccination. Unfortunately, little evidence of anti-cancer activity was seen in these mostly heavily pre-treated and advanced cancer patients. Pre-clinical trial have shown that the combination of the two vaccines generated a more potent response. In addition, IL-2 and GM-CSF have been shown to further stimulate the immune response to these vaccines. Our hope is that combining these agents will result in a well tolerated but significantly more potent immune stimulation targeting the CEA protein, and that we will be able to distinguish between the immunologic activity of the treatment arms.

The impact of such a trial may be great with broad reaching impact on a variety of common, lethal diseases.